Epitomes

Important Advances in Clinical Medicine

Ophthalmology

Fox Boswell, MD, Section Editor

The Council on Scientific Affairs of the California Medical Association presents the following epitomes of progress in ophthalmology. Each item, in the judgment of a panel of knowledgeable physicians, has recently become reasonably firmly established, both as to scientific fact and clinical importance. The items are presented in simple epitome, and an authoritative reference, both to the item itself and to the subject as a whole, is generally given for those who may be unfamiliar with a particular item. The purpose is to assist busy practitioners, students, researchers, and scholars to stay abreast of progress in medicine, whether in their own field of special interest or another.

The epitomes included here were selected by the Advisory Panel to the Section on Ophthalmology of the California Medical Association, and the summaries were prepared under the direction of Fox Boswell, MD, and the panel.

New Therapies for Cytomegalovirus Retinitis in Patients With the Acquired Immunodeficiency Syndrome

RECENT ESTIMATES suggest that the human immunodeficiency virus (HIV) has infected nearly 1 million people in the United States and more than 20 million worldwide. In as many as 70% of patients infected with the virus, one or more ocular complications will eventually develop, most often an opportunistic infection or unusual neoplasm. Cytomegalovirus (CMV) retinitis is the most common ocular infection in patients infected by HIV, affecting up to 40% of patients at some point during the course of their illness. Cytomegalovirus retinitis occurs almost exclusively in patients with $CD4^+$ T-lymphocyte counts below 100×10^6 per liter (100 cells per mm^3) and often affects both eyes.

Until recently, intravenous ganciclovir and foscarnet were the only agents approved by the Food and Drug Administration (FDA) for the treatment of active CMV retinitis. Although these therapies are effective at delaying the progression of disease, reactivation is the rule. In addition, the daily intravenous administration of ganciclovir and foscarnet is expensive, inconvenient, and frequently associated with adverse systemic side effects, most typically neutropenia and nephrotoxicity. Moreover, as patient survival and length of therapy have increased, viral resistance to these drugs has become more common.

The Studies of Ocular Complications of AIDS [acquired immunodeficiency syndrome] (SOCA) Research Group recently reported on the combined use of intravenous ganciclovir and foscarnet. Although combination therapy showed increased effectiveness at delaying the progression of retinitis, more than doubling the time to reactivation, treatment required daily, separate intravenous infusions. Most patients found this regimen difficult, with a substantially adverse effect on their overall quality of life. For this reason, combination therapy is usually reserved for those patients with severe systemic disease that is resistant to monotherapy alone.

Cidofovir, a new nucleotide analogue, recently gained approval from the FDA for the treatment of active CMV retinitis and appears to be as effective as either ganciclovir or foscarnet at preventing disease progression. In addition, cidofovir has two notable advantages: First, its exceedingly long intracellular half-life allows for weekly induction and every-two-weeks maintenance infusions, a treatment schedule that eliminates the need for an indwelling catheter. Second, cidofovir is effective against most viral strains that are resistant to ganciclovir and foscarnet and, as such, promises to play an increasingly important role in the treatment of long-standing disease. Cidofovir is, however, extremely nephrotoxic, prohibiting its use in patients with preexisting renal disease. Moreover, the intravenous administration of cidofovir is time-consuming and must be accompanied by aggressive hydration therapy and the use of probenecid to minimize renal toxicity. Cidofovir should, therefore, always be administered in a carefully controlled manner and patients monitored closely for side effects, including renal failure, neutropenia, neuropathy, alopecia, nausea, rash, and intraocular hypotony and uveitis. Cidofovir should not be used in patients prone to dehydration.

Oral ganciclovir has been approved by the FDA for use as maintenance therapy for inactive CMV retinitis. Whereas oral ganciclovir is effective at delaying the progression of inactive retinitis, the time to reactivation may be somewhat shorter, and the occurrence of new lesions in the uninvolved eye slightly more common with the use of oral versus intravenous drug. For patients with CMV retinitis not immediately threatening the optic nerve or macula, however, or for whom daily intravenous therapy is difficult or impossible, oral ganciclovir may offer a reasonable alternative. Oral ganciclovir is poorly absorbed by the gastrointestinal tract, and its use should be avoided in patients with diarrhea or poor gastrointestinal absorption.

Ophthalmologists routinely use the direct intraocular